REMARKS

I. Introduction

As a preliminary matter, applicants respectfully request that the examiner acknowledge an IDS that was filed on September 27, 2002.

Receipt is acknowledged of a non-final office action dated June 30, 2004. In the action, claim 1, 22, 24-25, and 28-44 were rejected as allegedly failing to meet the written description requirement, claim 8 was rejected as allegedly indefinite, and claims 1-6 and 22 were rejected as allegedly anticipated by Larsen *et al.*, WO 98/08949 ("Larsen"), Fell *et al.*, U.S. Patent 5,314,995 ("Fell"), Sissom *et al.*, Am. J. Pathol. 133:589 (1988) ("Sissom"), or Gillies *et al.*, *J. Immunol.*, 160:6195 (1998) ("Gillies"). Claims 7-9 were also objected to for formality reasons.

Applicants respectfully request reconsideration of the present application in view of the foregoing amendments and for the following reasons.

II. Status of the Claims

In this response, claim 2 has been canceled and claims 1 and 28 have been amended. Also, claim 22 has been revised to correct a typographical error, and claims 7-9 and 24 have been rewritten in independent form. Also, new claims 45-57 have been added. Support for the amended claims can be found in the original claims and on pages 18-19, paragraphs 54-55, of the present application. Support for the new claims can be found on page 12-13, paragraphs 40-42 and on page 17, paragraph 49 of the present specification. Upon entry of this amendment, claims 1-10, 22, 24, 25, and 28-57 will be under examination.

III. Rejection of the Claims under 35 U.S.C. § 112, 2nd Paragraph

Claim 8 was rejected under 35 U.S.C. § 112, 2nd paragraph as allegedly indefinite. Specifically, the claim was rejected allegedly because there is insufficient antecedent basis for the term "prolactin domain." Office action at 3. Applicants are unclear as to this rejection since claim 8 as filed in applicants last response of November 14, 2002 recites a "prolactin-antagonist

domain" and does not mention a "prolactin domain." Accordingly, applicants respectfully request withdrawal of the present rejection.

IV. Rejection of the Claims under 35 U.S.C. § 112, 1st Paragraph

Receptor-antagonizing domains, apoptosis promoting domains, and positive immunomodulator domains are adequately described in the instant application

Claims 1, 22, 24-25, and 28-44 were rejected under 35 U.S.C. § 112, 1st paragraph as allegedly failing to comply with the written description requirement. In particular, claims 1, 22-24, and 28-44 were rejected because "the case is not commensurate in scope to claims that read on a protein comprising any receptor-antagonizing domain or any apoptosis-promoting domain and any positive immunomodulatory domain." Office action at 3-4. However, the Office stated that the specification "set[s] forth a protein comprising 1) a prolactin-anta[g]onizing domain of SEQ Id No:1; and 2) a[n] immunomodulatory domain that is a cytokine" as well as "a fusion protein of hPRLA-IL2." Office action at 3.

The terms "receptor-antagonizing domain," "apoptosis-promoting domain" and "positive immunomodulatory domain" are domains that are identified by their function, *i.e.*, receptor antagonism, apoptosis induction, and positive immunomodulation. Specification at 14, paragraph 43. A skilled artisan would know how to assay such candidate domains based on the teachings in the art and the present specification. See, for example, paragraphs 87 and 88, and examples 5 and 6 on pages 35-36 of the specification.

Additionally, the specification, beginning on page 10, describes a receptor antagonizing domain and an apoptosis promoting domain. In additional to functional language, structural guidance is provided in the present application. See, specification at 12-13, paragraphs 39-41, and page 14, paragraph 44 to page 17, paragraph 48.

The present application also describes agents that induce apoptosis by positive means, *i.e.*, that induce an apoptotic pathway. Specification at 17, paragraph 50. Specific examples of such agents and the mechanism by which they act are described on pages 17-18, paragraphs 51 and 52 of the specification.

Furthermore, it is unclear why claim 25 was rejected for this reason since it is claimed that the "apoptosis-promoting domain inhibits STAT 3 phosphorylation in a cell." Thus, in addition to reciting a function (*i.e.*, causing apoptosis), the mechanism by which the apoptosis promoting domain works is described. Indeed, the Guidelines for satisfying the written description requirement, as cited in the office action, state that "the written description requirement for a claimed genus may be satisfied through . . . disclosure of relevant identifying characteristics, i.e., structure or other physical or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics." Office action at 4. Accordingly, recitation of an apoptotic function, in addition to the inhibition of a STAT 3 phosphorylation signaling pathway, is sufficient to satisfy the written description requirement.

Moreover, one of skill in the art could readily assay whether or not a candidate apoptosis promoting domain inhibited STAT 3 phosphorylation. For example, the STAT 5 immunoprecipitation assay described in Example 5 of the present application is applicable to STAT 3 proteins and to measurement of phosphorylation of other proteins as well.

Accordingly, receptor-antagonizing domains, apoptosis promoting domains, and positive immunomodulator domains are adequately described in the instant application.

Prolactin antagonizing domains comprising a truncated prolactin sequence are sufficiently described in the present application

The claims were also rejected because "with the exception of SEQ ID NO: 1, the skilled artisan cannot envision the detailed structure of the encompassed polypeptide [*i.e.*, one with a truncated prolactin sequence]." Office action at 6. Applicants respectfully disagree

As discussed in detail above, the present application sufficiently discloses variants of a prolactin-antagonist domain, including those that describe a truncated prolactin sequence. For example, the specification discloses regions of the prolactin antagonist domain that confer its antagonistic activity. Specification at 14, paragraph 42. For example, substituting residue 129 should produce a PRLA. *Id.* As such, one of skill in the art, based on the teachings in the present specification would know which regions can be removed from a prolactin sequence in the

prolactin antagonist domain to produce a PRLA, for example, that is suitable for use in the present invention. A skilled artisan would know how to assess that activity based on the assays disclosed in the present application. *Infra*. Accordingly, a prolactin antagonist domain comprising a truncated prolactin sequence.

"To which the apoptosis-promoting domain binds" is not new matter

Claim 25 was also separately rejected as allegedly containing new matter. In particular, the claim was rejected for reciting "to which the apoptosis-promoting domain binds." Office action at 2. Applicants respectfully disagree.

The specification, beginning on page 11, paragraph 37, sets forth the role of an apoptosis-promoting domain. In fact, the specification provides that an apoptosis-promoting domain can be a prolactin antagonist domain and the specification describes that the prolactin antagonist domain promotes apoptosis by blocking a prolactin receptor. Blocking the prolactin receptor occurs by binding of the prolactin receptor antagonist to the prolactin receptor. Indeed, the specification states that

> a suitable PRLA . . . generally will retain the characteristic of specific binding to the PRLR, yet will have some structural deficiency that disrupts the normal PRL apoptosis-blocking mechanism. Such a structural deficiency includes those that disrupt PRL (and thus PRLR) dimerization.

Specification at 12, paragraph 39. Therefore, for a prolactin receptor antagonist to promote apoptosis of a cell, it has to bind to the cell. As such, the phrase "to which the apoptosis-promoting domain binds" is not new matter.

V. Rejection of the Claims under 35 U.S.C. § 102(b)

Claims 1-6 and 22 were rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Larsen, Fell, Sissom, and/or Gillies. Essentially, the examiner asserted that the claimed invention reads on the fragments taught by Larsen and the antibodies described in Fell, Sissom, and Gillies. Applicants respectfully disagree.

The present invention discloses a method for treating cancer comprising administering a protein that comprises a receptor-antagonizing domain and a positive immunomodulator domain. As described in the specification, a receptor-antagonizing domain "binds to and antagonizes its cognate receptor" (specification at 11, paragraph 35). Cognate is understood by one of skill in the art to refer to two or more biomolecules that typically interact (*e.g.*, a receptor and its ligand). Applicants respectfully assert that an antibody functions to bind its antigen, not a receptor *per se*. Indeed, while an antibody may bind an ***antigen*** that is located on a receptor or other protein, an antigen is not understood by one of skill in the art, to be an antibody's cognate receptor.

In addition, Sissom does not teach a composition comprising a receptor antagonizing domain and a separate immunomodulator domain, wherein the immunomodulator domain is a cytokine.

Nevertheless, in the interest of expediting prosecution, applicants amended claim 1 to incorporate the features of claim 2 and canceled claim 2. Thus, claims 1, 3-6 and 22 do not read on the cited art.

Therefore, for at least these reasons, withdrawal of the rejections and reconsideration of the application is respectfully requested.

CONCLUSION

Reconsideration of the present application in view of the foregoing amendments and arguments is kindly requested.

It is respectfully urged that the present application is now in condition for allowance. Early notice to that effect is earnestly solicited.

Examiner Yaen is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

Respectfully submitted,

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